An Approach to the Total Synthesis of the Prelog–Djerassi Lactone

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An approach to the synthesis of the Prelog–Djerassi lactone using D-glucose as a starting material is described. The use of Swern oxidation provides an efficient means of preparing carbohydrate ketones. An unusual departure from the normal reaction pathway of the Peterson reaction has been observed, and has been found to depend on the stereochemistry of the intermediate β-hydroxysilanes.

Since its isolation from the degradation products of methynolide,[1] the Prelog–Djerassi lactone (**5**) has acquired considerable importance as a target in synthetic organic chemistry. It has been used both as an intermediate in the synthesis of macrolides and as a target for the demonstration of new synthetic techniques. This has led to a large number of published syntheses.[2]

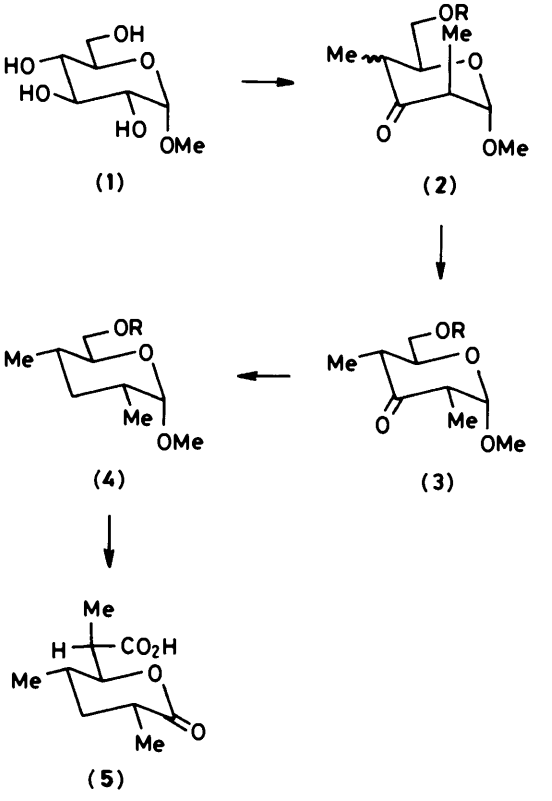
The stereochemistry of the compound was partially assigned by Djerassi,[3] who correctly assigned the C-4 and C-6 centres† as *S* and *R* respectively. Bergelson and Batrakov assigned the remaining stereocentres as 2*S* and 3*R*.[4] In 1970 Rickards re-examined the structure of the molecule and reversed the assignment on the basis of ^{1}H n.m.r. data.[5] The stereochemistry has now been confirmed as 2*R*,3*S*,4*S*,6*R* by several syntheses of the compound in its natural optically active form.

A particularly appealing approach to the synthesis of compound (**5**) is to use a carbohydrate as a starting material. The carbohydrate can then provide the basic skeleton of the molecule, leaving only extention from C-6 (carbohydrate numbering) and the introduction of the ring methyl groups in the correct stereochemistry. This latter task is aided by the fact that the two *C*-methyl groups are in the most thermodynamically stable orientation. This paper describes the work we have done towards the preparation of the Prelog–Djerassi lactone from D-glucose. Several syntheses of compound (**5**) from carbohydrates appeared while this work was in progress.[2p–r]

Results and Discussion

Our strategy (Scheme 1) was based on the idea that the stereochemistry of the C-2 and C-4 stereocentres (henceforth all numbering will correspond to the carbohydrate system) could be corrected at a late stage in the synthesis by a base-catalysed epimerization [(**2**) ⟶ (**3**)]. Thus a ketone similar to (**2**) would be prepared from methyl α-D-glucopyranoside (**1**), and then epimerized to give compound (**3**), which would in turn be reduced to compound (**4**). Extension from C-6 would then lead to the target molecule (**5**). A synthesis of the Prelog–Djerassi lactone from the intermediate (**4**; R = CPh_3) has been reported.[2q]

The C-2 methyl group was introduced by ring opening of the epoxide (**6**) (according to Fraser–Reid).[6] The epoxide (**6**) could be prepared in high yield by either of two routes (75% over three steps).[7,8] When compound (**6**) was treated at 0 °C in diethyl ether with lithium dimethylcuprate, formed *in situ* from methyllithium and copper(I) iodide, two products were isolated, the desired diaxial ring-opened product (**7**) in 65% yield and the glycal (**8**) in 9% yield. The by-product (**8**) presumably arises from attack of iodide ion on compound (**6**) and subsequent elimination. An iodohydrin has been isolated by Lemieux under similar reaction conditions.[9] A variety of experimental variations on the original method were made, but we were unable to prevent the formation of glycol (**8**). After manipulation of the various protecting groups, the benzyl ethers (**10**) were obtained in good overall yield (25% over 7 steps) (Scheme 2).

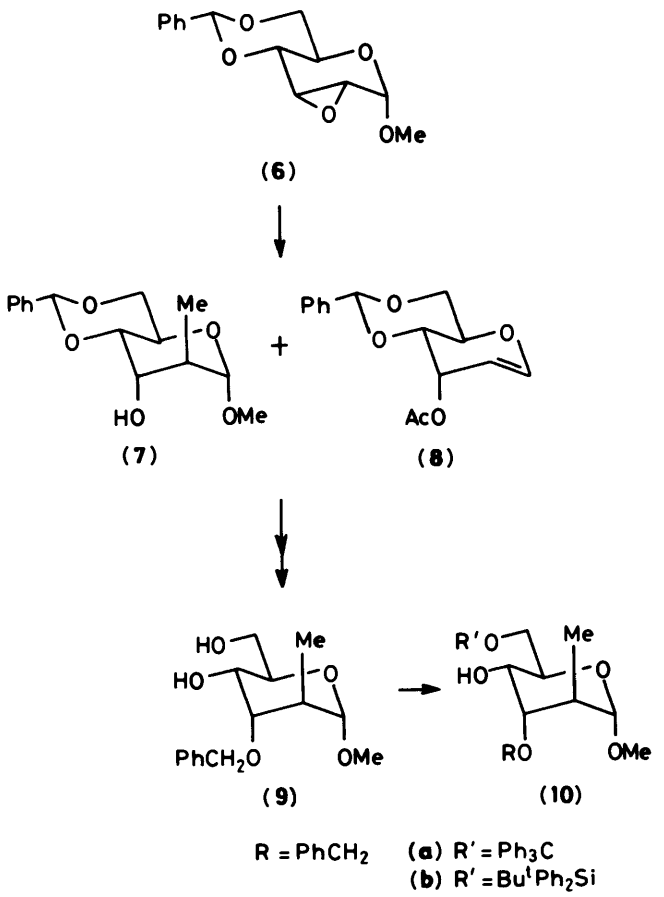


Scheme 1.

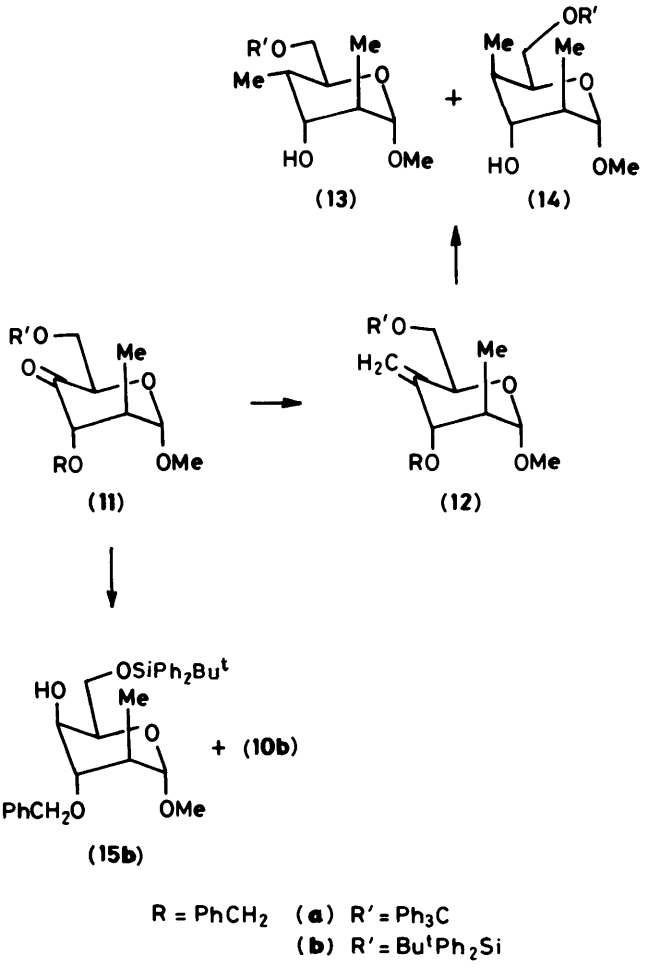
The second methyl group was to be introduced by oxidation of alcohol (**10**) to ketone (**11**), methylenation to give compound (**12**), and hydrogenation of the olefin (**12**) simultaneously to saturate the exocyclic double bond and to remove the benzyl protecting group. Each of these steps proved far more diffucult than was originally expected.

The alcohol (**10**) proved remarkably resilient to oxidation. When treated with pyridinium chlorochromate at a variety of temperatures and in a selection of solvents, either with or without molecular sieves,[10] the starting material (**10**) was recovered unchanged. Similarly, Collins reagent was completely ineffective.[11] We then turned to oxidation with dimethyl sulphoxide (DMSO) and a variety of activating agents.[12] Although phosphorus pentaoxide and acetic anhydride were

† For this discussion of the stereochemistry of lactone (**5**), C-1 is taken as the carboxylic acid carbon.



Scheme 2.



Scheme 3.

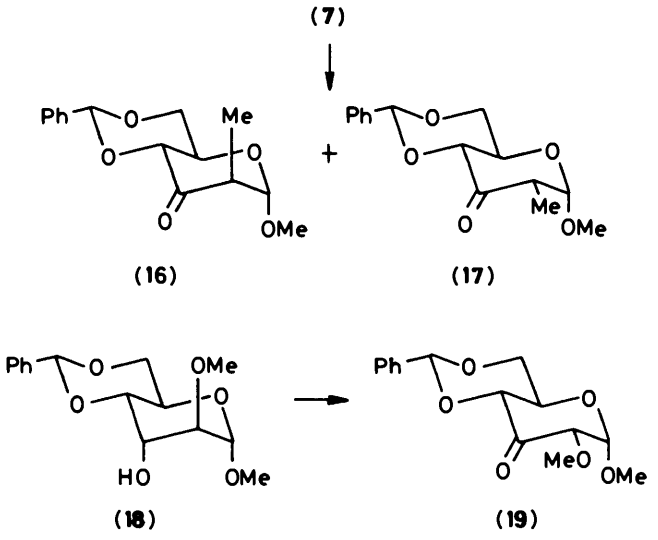
Table.

Substrate	1-H	2-H	3-H	5-H	6-H
(11a)	4.67, d $J_{1,2}$ 5.0 Hz	2.05, m	4.19, dd $J_{2,3}$ 12.0 Hz $J_{3,5}$ 1.0 Hz	4.30, br t $J_{5,6}$ 3.7 Hz	3.47, d $J_{5,6}$ 3.7 Hz
(11b)	4.65, d $J_{1,2}$ 5.0 Hz	2.05, m	4.08, dd $J_{2,3}$ 10.5 Hz $J_{3,5}$ 1.0 Hz	4.25, m	3.93—4.13 ABd $J_{6,6}$ 11.0 Hz $J_{5,6ax}$ 4.0 Hz $J_{5,6eq}$ 2.0 Hz

poor activators, Swern's method,[13] using oxalyl dichloride and quenching with triethylamine, gave good yields of ketone (**11**). The reaction was carried out under a nitrogen atmosphere and the temperature was carefully maintained at −30 °C. If the temperature of the reaction mixture rose above −40 °C, the protecting groups were cleaved, whereas if the temperature fell below −70 °C little or no reaction took place.

When the ^{1}H n.m.r. spectrum of compound (**11**) was examined (Table) a four-bond coupling between 3-H and 5-H was observed. The assignment of the spectrum was confirmed by decoupling experiments. While long-range couplings across carbonyl groups in cyclic compounds are quite common, the coupling protons usually adopt a W or U configuration (*i.e.* they are arranged in a di-equatorial or di-axial orientation).[14] For 3-H and 5-H of compound (**11**) to adopt either of these conformations, epimerization at C-3 or at C-5 is required. While epimerization at C-5 during the oxidation was thought to be unlikely, inversion of the stereochemistry at C-3 was quite possible. This possibility was further suggested by the large coupling constants observed between 2-H and 3-H of (**11a**) and (**11b**), consistent with a diaxial orientation. However, the simple expedient of reducing compound (**11b**) with sodium borohydride showed that no epimerization had occurred, as a mixture of compound (**10b**) and another compound, assigned by ^{1}H n.m.r. spectroscopy as having structure (**15b**), was obtained. The reason for this anomalous long-range coupling remains unclear.

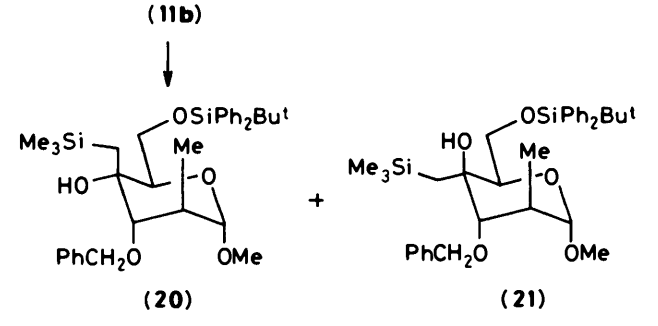
Having established that both (**10a**) and (**10b**) could be successfully oxidized by Swern's methods without epimerization at C-3 or C-5, we examined the oxidation of the alcohols (**7**) and (**18**) to determine whether oxidation without epimerization was general for this reagent. Oxidation of compound (**7**) gave a 73% yield of the ketone (**16**). Examination of the ^{1}H n.m.r. spectrum of the product showed that it was contaminated with ~6% of its isomer (**17**). On the other hand, oxidation of compound (**18**) gave the C-2-epimerized product (**19**) as the only product (Scheme 4). The assignment of the stereochemistry of compound (**19**) was based on analysis of the ^{1}H n.m.r. spectrum. In particular the coupling constant between 1-H and 2-H was 4.5 Hz, indicating an axial–equatorial relationship between the coupling protons. A long-range coupling between 2-H and 4-H of 1.5 Hz was also observed. We also examined the use of trifluoroacetic anhydride (TFAA) as an activator in the oxidation of compound (**10b**),[15] but this reagent was less effective, as starting material was recovered from the reaction



Scheme 4.

mixture after the reaction time usually allowed for the Swern method.

A successful method for the preparation of compound (**11**) led us to examine the preparation of the alkene (**12**). The Wittig reaction would have been an obvious choice of method for the conversion of (**11**) into (**12**); however, this led to problems of purification involving, in particular, separation of triphenylphosphine oxide from the olefinic product. The Peterson reaction was therefore selected,[16] a reaction which, at that time, had not been applied to carbohydrate derivatives. Recently a report of the use of the reaction of carbohydrates has appeared.[17] Treatment of compound (**11b**) with the Grignard reagent derived from (chloromethyl)trimethylsilane, followed by treatment with potassium hydride, gave a disappointing 35% yield of compound (**12b**). When the mixture of β-hydroxysilanes (Scheme 5) was treated with thionyl chloride the olefin (**12b**) was obtained,[18] but again in low yield (50%).



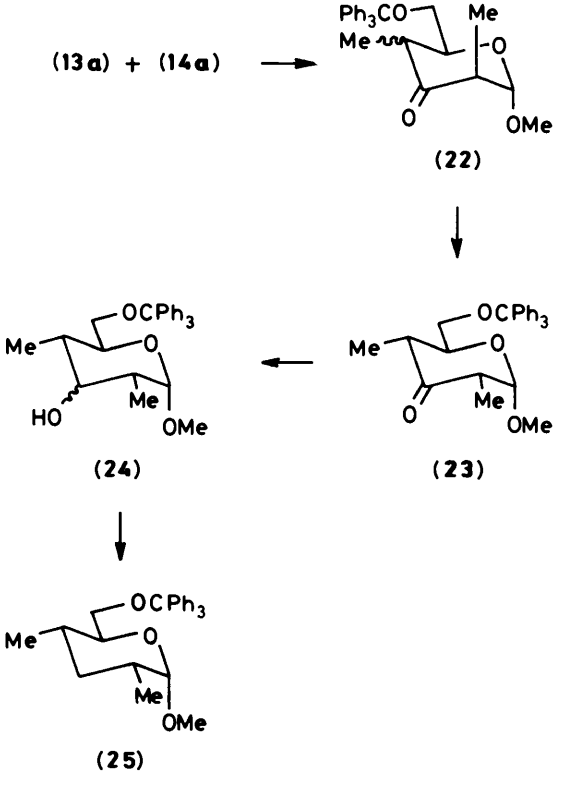
Scheme 5.

In an attempt to identify the reason for the failure of this Peterson reaction, the two diastereoisomeric β-hydroxysilanes (**20**) and (**21**) were isolated and separated by column chromatography. Determination of the C-4 stereochemistry of the two products were difficult, but was tentatively established by comparison of the ^{1}H n.m.r. spectra of compounds (**20**) and (**21**) with those of (**15b**) and (**10b**). The benzylic protons of all four compounds resonated as AB quartets. In the case of (**10b**) the two arms of the AB quartet were separated by 0.2 p.p.m., while those of (**15b**) were separated by only 0.05 p.p.m. Examination of the spectra of compounds (**20**) and (**21**) showed that in one compound the same set of peaks were separated by 0.2 p.p.m. while in the other the separation was only 0.03 p.p.m. On this basis the major isomer was assigned the structure (**21**), and the minor isomer structure (**20**).

The two diastereoisomers were treated separately with potassium hydride. The derivative with *altro* stereochemistry, (**20**), smoothly eliminated trimethylsilanol to give the olefin (**12b**), while the *ido* diastereoisomer (**21**) followed an alternative reaction pathway and gave a complex mixture of unidentified products. As far as can be determined this is the first time that two diastereoisomeric β-hydroxysilanes have followed different pathways during the elimination section of a Peterson reaction.

After the failure of the Peterson reaction, the olefins (**12a**) and (**12b**) were obtained by a Wittig reaction of the ketones (**11**) (in 84 and 57% yield respectively). The original intention was to remove the benzyl protecting group of compound (**12b**) and simultaneously to saturate the exocyclic olefin by hydrogenolysis on a palladium catalyst. This intention was frustrated by the fact that the diphenyl-t-butylsilyl protecting group was unstable under the reaction conditions. Although the olefinic function of compound (**12b**) could be saturated quite rapidly, the extended reaction time required to remove the benzyl group led to partial reduction of the silyl protecting group. We therefore abandoned the silyl-protected compound and examined the hydrogenation of the tritylated derivative (**12a**). Selective hydrogenation of this compound was possible giving a modest yield of a 2:1 mixture of (**13a**) and (**14a**), with the latter in excess. The stereochemical assignments were based on the values of the 4-H–5-H coupling constants, which in the case of the major product was 5 Hz, indicating an axial–equatorial relationship between the coupling protons, and in the case of the minor product was 10 Hz, indicating an axial–axial relationship.

The diastereoisomers (**13a**) and (**14a**) were oxidized separately to give the ketones (**22**). Analysis of the ^{1}H n.m.r. spectra



Scheme 6.

of these ketones confirmed the stereochemical assignments previously made and also showed that no epimerization had taken place during the oxidation.

The ketones (**22**) were treated with sodium methoxide in methanol at room temperature. Three products were observed, in approximately equal proportions, by t.l.c. When the reaction mixture was cooled to −78 °C a major product (**23**) became evident. This mixture was not separated, but was reduced with sodium borohydride, and a mixture of C-3 alcohols separated, in which compound (**24**) was thought to be the major product. The mixture was deoxygenated by the Barton–McCombie protocol[19] to give a 2:1 mixture of compound (**25**) and its C-4 epimer, which was isolated but not separated by preparative-scale t.l.c. (p.l.c.) (see Scheme 6).

Conclusion

This approach to the Prelog–Djerassi lactone (**5**) has led to several valuable insights into synthetic chemistry using carbohydrates. The Swern technique has proved useful in the oxidation of carbohydrate derivatives, but it is apparent that epimerization at the positions adjacent to the newly formed ketone can occur. The unusual course of the Peterson reaction reported herein has not, to our knowledge, been reported before and warrants further examination. Finally the diphenyl-t-butylsilyl group has been found to be unstable to hydrogenolysis over palladium.

Experimental

I.r. spectra were recorded on a Perkin-Elmer 297 instrument, with polystyrene (1 601 cm^{-1}) as standard. U.v. spectra were recorded on a Perkin-Elmer lambda 5 instrument. ^1H N.m.r. spectra were recorded at 250 MHz on a Bruker WM250 instrument for $CDCl_3$ solutions with tetramethylsilane as internal standard. $^N\delta_H$ refers to the ^1H n.m.r. spectrum measured after the addition of trichloroacetyl isocyanate. ^{13}C N.m.r. spectra were measured at 22.6 MHz on a Bruker HFX90 instrument for $CDCl_3$ solutions with tetramethylsilane as internal standard. Mass spectra were recorded on an A.E.I. MS30 instrument. M.p.s were measured on a Gallenkamp heated block apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 141 automatic polarimeter, using a 10 cm cell. All column chromatography was carried out according to ref. 20 on Merck 60 (230—400 mesh) silica gel. P.l.c. was carried out on 2 mm glass-backed plates, prepared with Merck 60 GF-254 silica gel. Analytical t.l.c. was carried out on Merck glass-backed t.l.c. plates, pre-coated with silica gel 60 F-254 to a depth of 0.2 mm. Light petroleum refers to that fraction boiling in the range 40—60 °C.

Methyl 4,6-O-*Benzylidene*-2-*deoxy*-2-C-*methyl*-α-D-*altropyranoside* (**7**).—Copper(I) iodide (10.9 g, 0.057 mol) was suspended in dry diethyl ether (100 ml) under nitrogen at 0 °C. Methyl-lithium (1.4M in diethyl ether) was added until the yellow colour originally formed was completely discharged to give a black solution. Methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (**6**) (10.0 g, 0.038 mol) was added and the reaction mixture was stirred for 5 h at 0 °C. The reaction mixture was poured into saturated aq. ammonium chloride, and stirred for 12 h. The product was then extracted into diethyl ether, and the extract was filtered through a pad of Celite, dried over potassium carbonate, and concentrated at reduced pressure. The residue was recrystallized from diethyl ether–light petroleum to give pure *compound* (**7**) (5.96 g, 56%), m.p. 104—107 °C; $[\alpha]_D^{20}$ +106° (*c* 1 in $CHCl_3$) {lit.,[6] m.p. 111—113 °C; $[\alpha]_D^{20}$ +120.8° (*c* 1 in $CHCl_3$)} (Found: C, 64.2; H, 7.3. $C_{15}H_{20}O_5$ requires C, 64.27; H, 7.19%); $\nu_{max.}$(mull) 3 502 cm^{-1} (O–H); $\lambda_{max.}(CH_3CN)$ 265 (ε 101), 261 (170), 255 (206), and 249 (155); δ_H 1.14 (3 H, d, *J* 8.0 Hz, 2-Me), 2.34 (1 H, qd, *J* 2.5 and 8.0 Hz, 2-H), 3.10 (1 H, d, *J* 6.6 Hz, O–H), 3.41 (3 H, s, OMe), 3.77 (1 H, dd, *J* 3.0 and 6.6 Hz, 4-H), 3.80 (1 H, t, *J* 10.0 Hz, 6-H_{ax}), 3.94 (1 H, dt, *J* 2.5, and 6.6 Hz, 3-H), 4.18—4.36 (2 H, m, 6-H_{eq} and 5-H), 4.51 (1 H, s, 1-H), 5.63 (1 H, s, PhC*H*), and 7.32—7.54 (5 H, m, Ph); $^N\delta_H$ 1.23 (3 H, d, *J* 7.7 Hz 2-Me), 2.50 (1 H, qd, *J* 2.2 and 7.5 Hz, 2-H), 3.36 (3 H, s, OMe), 3.78 (1 H, t, *J* 10.0 Hz, 6-H_{ax}), 3.94 (1 H, dd, *J* 3.0 and 9.5 Hz, 4-H), 4.3 (2 H, m, 6-H_{eq} and 5-H), 4.45 (1 H, s, 1-H), 5.13 (1 H, t, *J* 2.6 Hz, 3-H), 5.61 (1 H, s, PhC*H*), and 7.26—7.47 (5 H, m, Ph); δ_C 14.6 (2-Me), 39.1 (C-2), 54.5 (OMe), 57.5 (C-3), 68.4 and 69.3 (C-4 and -5), 75.8 (C-6), 101.3 (PhC*H*), 125.4 and 127.2 (*o*- and *m*-aromatics), 128.1 (*p*-aromatic), and 136.5 (*i*-aromatic); *m/z* 280 (M^+) and 248 ($M^+ - CH_3OH$).

The mother liquors from the recrystallization were dissolved in pyridine (125 ml) and acetic anhydride was added until t.l.c. [(2:1) light petroleum–ethyl acetate] showed all the by-product was acetylated. The mixture was stirred overnight with methanol, and was then concentrated under reduced pressure, and the residue was chromatographed [(2:1) light petroleum–ethyl acetate] to give, after crystallization from light petroleum–ether, a further crop of methyl 4,6-*O*-benzylidene-2-deoxy-2-C-methyl-α-D-altropyranoside (**7**) (1.0 g, 9.4%; total yield 65.4%), and 3-*O*-acetyl-4,6-*O*-benzylidene-1,2-dideoxy-D-*ribo*-hex-1-enopyranose (**8**) (0.9 g, 8.6%), m.p. 117—118 °C; $[\alpha]_D^{20}$ +254.8° (*c* 1 in $CHCl_3$) {lit.,[6] m.p. 120—121 °C; $[\alpha]_D^{20}$ +237° (*c* 0.17 in EtOH)}; $\nu_{max.}$(mull) 1 763 (C=O) and 1 633 cm^{-1} (enol ether); $\lambda_{max.}(CH_3CN)$ 265 (124), 259 (190), 255 (226), and 249 nm (176); δ_H 2.08 (3 H, s, Ac), 3.82 (1 H, t, *J* 10.0 Hz, 6-H_{ax}), 3.95 [1 H, dd, *J* 4.0 and 10.0 Hz (dec. at δ 5.4, d, *J* 10.0 Hz), 4-H], 4.17 (1 H, td, *J* 5.0, and 10.0 Hz, 5-H), 4.45 (1 H, dd, *J* 5.0 and 10.0 Hz, 6-H_{aq}), 5.00 ([1 H, t, *J* 6.0 Hz (dec. at δ 5.4, d, *J* 6.0 Hz), 2-H], 5.42 [1 H, dd, *J* 4.0 and 6.0 Hz (dec. at δ 5.00, d, *J* 4.0 Hz) 3-H], 5.59 (1 H, s, PhC*H*), 6.48 ([1 H, d, *J* 6.0 Hz (dec. at δ 5.00, s), 1-H], and 7.32—7.52 (5 H, m, Ph); δ_C 21.1 (q, CO*Me*), 61.9 and 64.9 (both d, C-4 and -5), 68.6 (t, C-6), 75.9 (d, C-3), 98.3 (d, C-2), 101.5 (d, PhC*H*), 126.0 and 128.2 (both d, *o*- and *m*-aromatics), 129.0 (d, *p*-aromatic), 137.0 (s, *i*-aromatic), 147.3 (d, C-1), and 170.5 (s, *C*OMe); *m/z* 276 (M^+).

Methyl 3-O-*Benzyl* -4,6-O-*benzylidene*-2-*deoxy*-2-C-*methyl*-α-D-*altropyranoside*.—Methyl 4,6-*O*-benzylidene-2-deoxy-2-C-methyl-α-D-altropyranoside (**7**) (1.0 g, 3.6 mmol) was dissolved in dry tetrahydrofuran (THF) (40 ml), and sodium hydride (60% dispersion in oil; 0.20 g, 5.1 mmol) and benzyl chloride (1.3 g, 10.2 mmol) were added. The mixture was refluxed for 18 h. The reaction was then quenched with methanol, and the mixture was diluted with water and extracted into dichloromethane. The extract was dried over sodium sulphate and concentrated under reduced pressure. The *title product* was obtained as a crystalline solid by flash chromatography (1.23 g, 94%), m.p. 97—100 °C; $[\alpha]_D^{20}$ +36° (*c* 1 in $CHCl_3$) (Found: C, 71.0; H, 7.1. $C_{22}H_{26}O_5$ requires C, 71.33; H, 7.07%); $\lambda_{max.}(CH_3CN)$ 261 (268), 256 (358), and 250 nm (257); δ_H 1.10 (3 H, d, *J* 7.7 Hz, 2-Me), 2.37 (1 H, dq, *J* 2.2 and 7.7 Hz, 2-H), 3.40 (3 H, s, OMe), 3.70 (1 H, m, 3-H), 3.74 (1 H, t, *J* 10.3 Hz, 6-H_{ax}), 3.83 (1 H, dd, *J* 2.9 and 9.6, Hz, 4-H), 4.32 (1 H, dd, *J* 5.2 and 10.3 Hz (6-H_{eq}), 4.42 (1 H, s, 1-H), 4.44 (1 H, td, *J* 5.2, and 10.0 Hz, 5-H), 4.79 and 4.82 (2 H, AB, *J* 13.0 Hz, PhCH_2), 5.56 (1 H, s, PhC*H*), and 7.23—7.53 (10 H, m, 2 × Ph); δ_C 16.5 (2-Me), 38.7 (C-2), 55.4 (OMe), 58.4, 69.6, 72.2, 76.2, and 77.3 (C-3, -4, -5, and 6, and Ph*C*H_2), 102.2 (PhCH), 103.0 (C-1), and 126.2—139.2 (aromatics); *m/z* 370 (M^+) and 388 ($M^+ - CH_3OH$).

Methyl 3-O-*Benzyl*-2-*deoxy*-2-C-*methyl*-α-D-*altropyranoside* (**9**).—Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-dexoy-2-C-

methyl-α-D-altropyranoside (14.0 g, 0.038 mol) was dissolved in methanol (1 l) and the solution was cooled to 0 °C. Toluene-*p*-sulphonic acid monohydrate (3.5 g, 0.018 mol) was added. The mixture was stirred at 0 °C for 3 h, after which t.l.c. [ethyl acetate–light petroleum (2:1)] showed the reaction was complete. The reaction was quenched when the mixture had been stirred overnight with solid sodium hydrogen carbonate. The reaction mixture was concentrated under reduced pressure and the residue was taken up in dichloromethane. After filtration, the mixture was again concentrated and the *title product* (**9**) was recrystallized from diethyl ether–light petroleum (8.53 g, 80%), m.p. 83—85 °C; $[\alpha]_D^{20}$ +13.4° (*c* 0.24 in $CHCl_3$) (Found: C, 63.7; H, 7.8. $C_{15}H_{22}O_5$ requires C, 63.81; H, 7.85%); $\nu_{max.}$($CHCl_3$) 3 540 and 3 450 cm^{-1} (O–H); $\lambda_{max.}$(CH_3CN) 263 (159), 257 (205), and 251 nm (178); δ_H 1.04 (3 H, d, *J* 7.7 Hz, 2-Me), 2.15 (1 H, t, *J* 5.5 Hz, 6-OH), 2.45 (1 H, m, 2-H), 2.65 (1 H, d, *J* 9.9 Hz, 4-OH), 3.37 (3 H, s, OMe), 3.57 (1 H, t, *J* 3.5 Hz, 3-H), 3.71—3.93 (4 H, m, 4- and 5-H, and 6-H_2), 4.41 and 4.79 (2 H, AB, *J* 11.4 Hz, PhCH_2), 4.43 (1 H, s, 1-H), and 7.35 (5 H, m, Ph); $^N\delta_H$ 1.12 (3 H, d, *J* 7.3 Hz, 2-Me), 2.30 [1 H, m, (dec. at δ 3.85 changes m), 2-H], 3.41 (3 H, s, OMe), 3.76 [1 H, dd, *J* 3.7 and 6.2 Hz (dec. at δ 5.2, d, *J* 6.2 Hz; dec. at δ 2.3, d, *J* 3.7 Hz), 3-H], 4.47 (4 H, m, 1- and 5-H, and 6-H_2), 4.53 and 4.63 (2 H, AB, *J* 11.7 Hz, PhCH_2), 5.21 [1 H, dd, *J* 3.7 and 7.31 Hz (dec. at δ 3.85, d, *J* 3.7 Hz), 4-H], 7.32 (5 H, m, Ph), and 8.52 and 8.56 (each 1 H, s, NH); δ_C 14.9 (2-Me), 34.4 (C-2), 54.8 (OMe), 62.4, 63.9, 69.4, and 70.5 (C-3, -4, -5, and -6), 78.11 (PhCH_2), 102.4 (C-1), and 127.5—137.8; *m/z* 282 (M^+) and 250 (M − CH_3OH).

After column chromatography [ethyl acetate–light petroleum (3:1)] of the mother liquors from the crystallization, a second crop of methyl 3-*O*-benzyl-2-deoxy-2-*C*-methyl-α-D-altropyranoside (**9**) (0.56 g, total yield 85%) was isolated. Another product (0.43 g, 4%) was also isolated and was identified as *methyl* 3-O-*benzyl*-2-*deoxy*-2-C-*methyl*-β-D-*altropyranoside*, $[\alpha]_D^{20}$ −2.4° (*c* 0.81 in $CHCl_3$); $\nu_{max.}$(film) 3 515 and 3 450 cm^{-1} (O–H); δ_H 0.99 (3 H, d, *J* 7.3 Hz, 2-Me), 2.35 (1 H, m, 2-H), 2.55 (2 H, br m, 4- and 6-OH), 3.48 (3 H, s, OMe), 3.66—3.89 (5 H, m, 3-, 4-, and 5-H, and 6-H_2), 4.68 and 4.71 (2 H, AB *J* 11.5 Hz, PhCH_2), 4.75 (1 H, s, 1-H), 7.34 (5 H, m, Ph); $^N\delta_H$ 1.04 (3 H, d, *J* 7.3 Hz, 2-Me), 2.35 (1 H, m, 2-H), 3.46 (3 H, s, OMe), 3.97 [1 H, dd, *J* 6.0 and 3.0 Hz (dec. at δ 5.15, d, *J* 6.0 Hz; dec. at δ 2.35, br s), 3-H], 4.29 (1 H, dt, *J* 5.0 and 7.0 Hz, 5-H), 4.45 and 4.51 (2 H, ABd, J_{AB} 11.5, $J_{5,6}$ 5.0 Hz, 6-H_2), 4.59 and 4.61 (2 H, AB, *J* 11.5 Hz, PhCH_2), 4.79 (1 H, d, *J* 2.8 Hz, 1-H), 5.18 (1 H, dd, *J* 3.0 and 7.3 Hz, 4-H), 7.32 (5 H, m, Ph), and 8.66 and 8.67 (each 1 H, s, NH); δ_C 9.6 (2-Me), 36.1 (C-2), 56.9 (OMe), 63.3, 64.8, 71.9, 75.8, and 80.6 (C-3, -4, -5, and -6, and PhCH_2), 101.2 (C-1), and 127.7—128.6 and 137.9 (aromatics); *m/z* 282 (M^+) (Found: M^+, 282.1471. $C_{15}H_{22}O_5$ requires *M*, 282.1467).

Methyl 3-O-*Benzyl*-2-*deoxy*-6-O-(*diphenyl*-t-*butylsilyl*)-2-C-*methyl*-α-D-*altropyranoside* (**10b**).—Methyl 3-*O*-benzyl-2-deoxy-2-*C*-methyl-α-D-altropyranoside (**9**) (3.0 g, 0.011 mol), imidazole (1.5 g, 0.022 mol), and diphenyl-t-butylsilyl chloride (3.5 g, 0.013 mol) were dissolved in dimethylformamide (DMF) (180 ml) and the solution was stirred for 12 h. The reaction was quenched with water and the mixture was concentrated under reduced pressure. The residue was partitioned between water and dichloromethane. The organic phase was separated, dried over sodium sulphate, and concentrated. The *title product* (**10b**) was obtained as a clear oil by flash chromatography [light petroleum–ethyl acetate (13:2)] (5.58 g, 97%), $[\alpha]_D^{20}$ +58.5° (*c* 1 in $CHCl_3$) (Found: C, 71.4; H, 7.7. $C_{31}H_{40}O_5Si$ requires C, 71.50; H, 7.74%); $\nu_{max.}$(film) 3 400 cm^{-1} (O–H); $\lambda_{max.}$(CH_3CN) 270 (571), 264 (820), 263 (784), 261 (729), 259 (805), and 254 nm (628); δ_H 1.05 (12 H, m, Bu^t and 2-Me), 2.35 (1 H, m, 2-H), 2.54 (1 H, d, *J* 8.0 Hz, 4-OH), 3.38 (3 H, s, OMe), 3.54 (1 H, t, *J* 4.0 Hz, 3-H), 3.9 (4 H, m, 4- and 5-H, and 6-H_2), 4.45 (1 H, d, *J* 2.2 Hz, 1-H), 4.44 and 4.72 (2 H, AB, *J* 11.3 Hz, PhCH_2), and 7.35 and 7.75 (total 15 H, m, 3 × Ph); $^N\delta_H$ 1.10 (12 H, m, Bu^t and 2-Me), 2.14 (1 H, m, 2-H), 3.41 (3 H s, OMe), 3.66 (1 H, dd, *J* 3.7 and 8.8 Hz, 3-H), 3.85 (2 H, d, *J* 4.4 Hz, 6-H_2), 4.17 (1 H, m, 5-H), 4.46 (1 H, s, 1-H), 4.50 and 4.60 (2 H, AB, *J* 11.3 Hz, PhCH_2), 5.51 (1 H, t, *J* 3.7 Hz 4-H), 7.28—7.74 (15 H, m, 3 × Ph), and 8.48 (1 H, s, NH); δ_C 15.1 (CMe_3), 19.2 (2-Me), 26.8 (CMe_3), 34.8 (C-2), 55.0 (OMe), 63.9, 64.3, 71.0, and 71.1 (C-3, -4, -5, and -6), 78.6 (PhCH_2), 102.7 (C-1), and 127.5—138.0 and 164.0 (aromatics); *m/z* 520 (M^+) and 489 (M^+ − CH_3O).

Methyl 3-O-*Benzyl*-2-*deoxy*-2-C-*methyl*-6-O-*trityl*-α-D-*altropyranoside* (**10a**).—Methyl 3-*O*-benzyl-2-deoxy-2-*C*-methyl-α-D-altropyranoside (**9**) (3.0 g, 10.6 mmol) was dissolved in dry pyridine (500 ml), and triphenylmethyl chloride (4.0 g, 14.3 mmol) was added. The reaction mixture was stirred at 70 °C until t.l.c. [light petroleum–ethyl acetate (2:1)] showed that the reaction was complete. The reaction was then quenched with water, and the mixture was concentrated under reduced pressure. The residue was partitioned between water and dichloromethane. The organic phases were separated, dried over sodium sulphate, and concentrated. The *title product* (**10a**) was obtained as an oil by flash chromatography [light petroleum–ethyl acetate (5:2)] (5.25 g, 95%), $[\alpha]_D^{20}$ +50.8° (*c* 0.8 in $CHCl_3$); $\nu_{max.}$(film) 3 539br cm^{-1} (O–H); δ_H 1.06 (3 H, d, *J* 7.3 Hz, 2-Me), 2.32 (1 H, m, 2-H), 2.46 (1 H, br d, *J* ~8 Hz, OH), 3.27 and 3.40 (2 H, ABd, J_{AB} 10.1, J_{ax} 6.5, J_{eq} 2.7 Hz, 6-H_2), 3.47 (3 H, s, OMe), 3.50 (1 H, m, 3-H), 3.70 (1 H, m, 4-H), 4.02 (1 H, m, 5-H), 4.45 and 4.70 (2 H, AB, *J* 11.5 Hz, PhCH_2), 4.47 (1 H, d, *J* 2.4 Hz, 1-H), and 7.20—7.52 (20 H, m, 4 × Ph); $^N\delta_H$ 1.07 (3 H, d, *J* 6.9 Hz, 2-Me), 2.22 (1 H, m, 2-H), 3.27 and 3.33 (2 H, ABd, J_{AB} 10.2, J_{ax} = J_{eq} 5.0 Hz, 6-H_2), 3.45 (3 H, s, OMe), 3.59 (1 H, dd, *J* 3.6 and 8.8 Hz, 3-H), 4.25 (1 H, q, *J* 5.0 Hz, 5-H), 4.43 (1 H, d, *J* 5.9 Hz, 1-H), 4.48 and 4.57 (2 H, AB, *J* 12.5 Hz, PhCH_2), 5.37 (1 H, dd, *J* 3.6 and 5.0 Hz, 4-H), 7.20—7.50 (20 H, m, 4 × Ph), and 8.35 (1 H, s, NH); δ_C 15.2 (2-Me), 34.9 (C-2), 55.0 (OMe), 64.5 (C-6), 70.3 and 70.9 (C-3 and -5), 78.6 (PhCH_2), 86.6 (C-4), 102.8 (C-1), and 126.8—138.2 (aromatics); *m/z* 524 (M^+) (Found: M^+, 524.2568. $C_{34}H_{36}O_5$ requires *M*, 524.2561).

Methyl 3-O-*Benzyl*-2-*deoxy*-2-C-*methyl*-6-O-*trityl*-α-D-arabino-*hexopyranosid*-4-*ulose* (**11a**).—Dry DMSO (60 ml) and dry dichloromethane (250 ml) were stirred at −60 °C under nitrogen and a solution of oxalyl dichoride (8.7 g, 0.069 mol) in dry dichloromethane (20 ml) was added dropwise during 10 min. After a further 10 min, a solution of methyl 3-*O*-benzyl-2-deoxy-2-*C*-methyl-6-*O*-trityl-α-D-altropyranoside (**10a**) (5.24 g, 1.0 mmol) in dichloromethane (20 ml) was added dropwise. The reaction mixture was stirred for 4 h, and was then poured into triethylamine (40 ml) at room temperature. After 15 min, the mixture was diluted with brine and the product was extracted into dichloromethane. The extracts were washed successively with water and brine, combined, and then dried over sodium sulphate. The solution was concentrated under reduced pressure, and the *title product* (**11a**) was obtained as an oil by flash chromatography [light petroleum–ethyl acetate (3:1)] (5.28 g, quantitative) (Found: C, 78.4; H, 6.5. $C_{34}H_{34}O_5$ requires C, 78.14; H, 6.54%); $\nu_{max.}$(film) 1 746 cm^{-1} (C=O); δ_H 1.36 [3 H, d, *J* 6.5 Hz (decoupling at δ 2.05 produced incomplete collapse), 2-Me], 2.05 (1 H, m, 2-H), 3.41 (3 H, s, OMe), 3.47 [2 H, d, *J* 3.7 Hz (dec. at δ 4.3, s), 6-H_2], 4.19 [1 H, dd, *J* 1.0 and 12.0 Hz (dec. at δ 4.3, d, *J* 12.0 Hz; dec. at δ 2.05, d, *J* 1.0 Hz), 3-H], 4.3 (1 H, br t, *J* 3.7 Hz, 5-H), 4.45 and 4.95 (2 H, AB, *J* 11.7 Hz, PhCH_2), 4.67 [1 H, d, *J* 5.0 Hz (dec. δ 2.05, s), 1-H], and 7.4 (20 H, m, 4 × Ph); δ_C 22.3 (q, 2-Me), 41.0 (d, C-2), 55.3 (q, OMe), 63.6 (t, C-6), 73.3 and 81.8 (both d, C-3 and -5), 75.7 (t, PhCH_2), 86.9 (CPh_3), 103.0 (d, C-1), 126—168 (aromatics), and 209.6 (s, C-4); *m/z* 522 (M^+) and 490 (M^+ − CH_3OH).

Methyl 3-O-*Benzyl*-2-*deoxy*-6-O-(*diphenyl*-t-*butylsilyl*)-2-C-*methyl*-α-D-arabino-*hexopyranosid*-4-*ulose* (**11b**).—(a) *With DMSO–oxalyl chloride.* Dry DMSO (9.0 g, 0.11 mol) was dissolved in dry dichloromethane (20 ml) at −60 °C under nitrogen, and a solution of oxalyl dichloride (1.45 g, 0.012 mol) in dry dichloromethane (6 ml) was added dropwise. The mixture was stirred for 20 min. A solution of methyl 3-*O*-benzyl-2-deoxy-6-*O*-(diphenyl-t-butylsilyl)-2-*C*-methyl-α-D-altropyanoside (**10b**) (0.65 g, 1.25 mmol) in dry dichloromethane (6 ml) was added dropwise. After 1 h, the reaction mixture was poured into triethylamine (4 ml) at room temperature. After 5 min, the mixture was diluted with brine, and the product was washed with water, dried over sodium sulphate, and concentrated under reduced pressure. The *title product* (**11b**) was obtained as an oil by flash chromatography [light petroleum–ethyl acetate (7:1)] (0.56 g, 86%), $\nu_{max.}$(CH_2Cl_2) 1 745 cm^{-1} (C=O); δ_H 1.05 (9 H, s, Bu^t), 1.25 (3 H, d, *J* 7.3 Hz, 2-Me), 2.05 (1 H, m, 2-H), 3.39 (3 H, s, OMe), 3.93 and 4.13 (2 H, ABd, J_{AB} 11.0, J_{eq} 2.0, J_{ax} 4.0 Hz, 6-H_2), 4.08 [1 H, dd, *J* 10.5 and 1.0 Hz (dec. at δ 2.05, d, *J* 1 Hz), 3-H], 4.25 (1 H, m, 5-H), 4.44 and 4.99 (2 H, AB, *J* 11.5 Hz, PhCH_2), 4.65 [1 H, d, *J* 5.0 Hz (dec. at δ 2.05 s), 1-H], and 7.3—7.75 (15 H, m, 3 × Ph); δ_C 16.2 (2-Me), 19.1 (*C*Me_3), 40.9 (C-2), 55.2 (OMe), 63.6 (C-6), 73.3 and 82.0 (C-3 and -5), 76.9 (Ph*C*H_2), 104.9 (C-1), 127.6—163.9 (aromatics), and 209.0 (C-4); *m/z* 518 (M^+) and 487 ($M^+ - OCH_3$) (Found: M^+, 518.2479. $C_{31}H_{38}O_5Si$ requires *M*, 518.2488).

(b) *With DMSO–TFAA.* Dry dichloromethane (2 ml) and freshly distilled DMSO (1.1 g, 14.0 mmol) were stirred at −60 °C under nitrogen, and a solution of TFAA (0.21 g, 1.0 mmol) in dry dichloromethane (0.5 ml) was added dropwise. After 5 min, a solution of methyl 3-*O*-benzyl-2-deoxy-6-*O*-(diphenyl-t-butylsilyl)-2-*C*-methyl-α-D-altropyranoside (**10b**) (0.056 g, 0.11 mmol) in dichloromethane (1 ml) was added dropwise. The reaction mixture was stirred at −60 °C for 1 h, and then poured into triethylamine (1 ml) at room temperature. After 15 min, the mixture was diluted with brine and the product was extracted into dichloromethane. The solution was dried over sodium sulphate, and concentrated under reduced pressure. The products were purified by p.l.c. [light petroleum–ethyl acetate 7:1)] to give compound (**11b**) (0.034 g, 60%) and unchanged starting material (0.014 g, 25%). The products were identified by n.m.r. comparison with authentic samples.

Reduction of Methyl 3-O-*Benzyl*-2-*deoxy*-6-O-(*diphenyl*-t-*butylsilyl*)-2-C-*methyl*-α-D-arabino-*hexopyranosid*-4-*ulose* (**11b**).—Methyl 3-*O*-benzyl-2-deoxy-6-*O*-(diphenyl-t-butylsilyl)-2-*C*-methyl-α-D-*arabino*-hexopyranosid-4-ulose (**11b**) (0.06 g, 0.12 mmol) was dissolved in methanol (5 ml), and sodium borohydride (0.008 g, 2.0 mmol) was added. After being stirred for 12 h, the mixture was poured into saturated aq. ammonium chloride. The product was extracted into dichloromethane. The extract was dried over sodium sulphate and concentrated under reduced pressure. High-field n.m.r. spectroscopy showed that the product was a 5:1 mixture of diastereoisomers. The products were separated by p.l.c. [light petroleum–ethyl acetate (5:1)]. The major product (0.02 g, 33%) was identical to methyl 3-*O*-benzyl-2-deoxy-6-*O*-(diphenyl-t-butylsilyl)-2-*C*-methyl-α-D-altropyranoside (**10b**) as determined by t.l.c. and n.m.r. comparison. The minor product was identified from its ^{1}H n.m.r. spectrum as methyl 3-*O*-benzyl-2-deoxy-6-*O*-(diphenyl-t-butylsilyl)-2-*C*-methyl-α-D-idopyranoside (**15b**), $^N\delta_H$ 1.05 (12 *H*, *m*, 2-Me and Bu^t), 2.05 (1 H, m, 2-H), 3.35 (3 H, s, OMe), 3.56 (1 H, t, *J* 4.0 Hz, 3-H), 3.77 (2 H, d, *J* 7.0 Hz, 6-H_2), 4.38 (1 H, td, *J* 7.7 and 2.5 Hz, 5-H), 4.68 (1 H, d, *J* 2.5 Hz, 1-H), 4.67 and 4.73 (2 H, AB *J* 12.0 Hz, PhCH_2), 5.19 (1 H, t, *J* 2.5 Hz, 4-H), 7.32—7.54 (15 H, m, 3 × Ph), and 8.45 (1 H, s, NH).

Methyl 4,6-O-*Benzylidene*-2-*deoxy*-2-C-*methyl*-α-D-arabino-*hexopyranosid*-3-*ulose* (**16**).—Dry dichloromethane (20 ml) and dry DMSO (10 ml) were stirred together at −60 °C under nitrogen, and a solution of oxalyl dichloride (0.8 ml, 1.13 g, 8.9 mmol) in dry dichloromethane (5 ml) was added dropwise. After 10 min a solution of methyl 4,6-*O*-benzylidene-2-deoxy-2-*C*-methyl-α-D-altropyranoside (**7**) (0.25 g, 0.89 mmol) in dry dichloromethane (5 ml) was added dropwise. After 2 h, the reaction mixture was poured into triethylamine (10 ml) at room temperature. After 5 min, the mixture was diluted with brine, and the product was extracted into dichloromethane. The extracts were washed with water, dried over sodium sulphate, and concentrated under reduced pressure. The *title product* (**16**) was obtained as an amorphous solid by p.l.c. [light petroleum–ethyl acetate (2:1)] (0.18 g, 73%), m.p. 173—178 °C; $[\alpha]_D^{20}$ +106.2° (*c* 0.41 in $CHCl_3$) (Found: C, 64.6; H, 6.6. $C_{15}H_{18}O_5$ requires C, 64.74; H, 6.52%); $\nu_{max.}$(mull) 1 730 cm^{-1} (C=O); δ_H 1.37 (3 H, d, *J* 7.8 Hz, 2-Me), 2.78 (1 H, q, *J* 7.8 Hz, 2-H), 3.37 (3 H, s, OMe), 3.93 (1 H, t, *J* 10.1 Hz, 6-H_{ax}), 4.15 (1 H, td, *J* 4.6, and 10.1 Hz, 5-H), 4.37 (1 H, dd, *J* 4.6 and 10.1, 6-H_{eq}), 4.48 (1 H, d, *J* 10.1 Hz, 4-H), 4.76 (1 H, s, 1-H), 5.58 (1 H, s, PhC*H*), and 7.32—7.54 (5 H, m, Ph); δ_C 8.6 (2-Me), 48.9 (C-2), 55.4 (OMe), 65.9 (C-5), 69.6 (C-6), 83.0 (C-4), 102.1 (Ph*C*H), 104.6 (C-1), 126.5—136.7 (aromatics), and 199.3 (C-3); *m/z* 278 (M^+) and 247 ($M^+ - OCH_3$).

Methyl 3-O-*Benzyl*-2,4-*dideoxy*-6-O-(*diphenyl*-t-*butylsilyl*)-2-C-*methyl*-4-C-*methylene*-α-D-arabino-*hexopyranoside* (**12b**).—(Chloromethyl)trimethylsilane (0.18 g, 1.4 mmol) was added to magnesium turnings (pre-activated with iodine; 0.07 g, 0.25 mmol based on m.w. on MgI_2) in dry diethyl ether (2 ml). The mixture was stirred for 1 h, and then a solution of methyl 3-*O*-benzyl-2-deoxy-6-*O*-(diphenyl-t-butylsily)-2-*C*-methyl-α-D-*arabino*-hexopyranosid-4-ulose (**11b**) (0.06 g, 0.12 mmol) in dry diethyl ether (1.5 ml) was added. The reaction mixture was stirred until t.l.c. [light petroleum–ethyl acetate (5:1)] showed that no starting material was present, and two new products had been formed. The reaction was quenched by addition of a little methanol, and was then diluted with water. The product was extracted with dichloromethane, and the extract was dried over sodium sulphate. The resulting solution was concentrated under reduced pressure. The product was then dissolved in dry THF (1 ml), and the solution was added to potassium hydride (35% dispersion in oil, pre-washed with light petroleum; 0.05 g, 0.44 mmol). After the mixture had been stirred for 30 min at 25 °C, a single product was detected by t.l.c. The reaction mixture was quenched with methanol and diluted with water. The product was extracted into dichloromethane, and the extract was dried over sodium sulphate and then concentrated under reduced pressure. The title product (**12b**) was obtained as an oil by p.l.c. [light petroleum–ethyl acetate (11:2)] (0.022 g, 35%), δ_H 1.03 (3 H, d, *J* 7.3 Hz, 2-Me), 1.09 (9 H, s, Bu^t), 2.00 [1 H, m (dec. at δ 1.02, dd, $J_{1,2}$ 3, $J_{2,3}$ 6 Hz), 2-H], 3.41 (3 H, s, OMe), 3.70 (1 H, br d, *J* 6 Hz, 3-H), 3.91 (2 H, ABd, J_{AB} 11, J_{ax} 6, J_{eq} 5 Hz, 6-H_2), 4.36 and 4.68 (2 H, AB, *J* 12 Hz, PhCH_2), 4.50 (1 H, d, *J* 3 Hz, 1-H), and 7.3—7.7 (15 H, m, 3 × Ph); δ_C 16.0 (2-Me), 19.3 (*C*Me_3), 26.8 (C*Me*$_3$), 42.2 (C-2), 55.5 (OMe), 65.6 (C-6), 70.7 and 71.0 (C-3 and Ph*C*H_2), 80.5 (C-5), 104.3 (C-1), 110.4 (C=*C*H_2), 127—136 (aromatics), and 133.5 (C-4).

Elimination of Thionyl Chloride.—Methyl 3-*O*-benzyl-2-deoxy-6-*O*-(diphenyl-t-butylsilyl)-2-*C*-methyl-α-D-*arabino*-hexopyranosid-4-ulose (**11b**) (0.05 g, 0.10 mmol) was stirred in dry diethyl ether (2 ml) at room temperature under nitrogen. Trimethylsilylmethylmagnesium chloride (1M in diethyl ether; 0.5 ml, 0.5 mmol) was added. After 90 min, the reaction was complete, as determined by t.l.c. [light petroleum–ethyl acetate (5:1)]. Thionyl chloride (0.0015 ml, 0.02 mmol) was added. When t.l.c. showed that the elimination was complete, the

mixture was concentrated under reduced pressure. The residue was taken up in dichloromethane and quenched by addition of saturated aq. sodium hydrogen carbonate. The product was extracted into dichloromethane, and the extract was dried over sodium sulphate and concentrated under reduced pressure to give methyl 3-*O*-benzyl-2,4-dideoxy-6-*O*-(diphenyl-t-butylsilyl)-2-*C*-methyl-4-*C*-methylene-α-D-*arabino*-hexopyranoside (**12b**) (0.02 g, 40%).

Alternative Preparation of Methyl 3-O-*Benzyl*-2,4-*dideoxy*-6-O-(*diphenyl-t-butylsilyl*)-2-C-*methyl*-4-C-*methylene*-α-D-arabino-*hexopyranoside* (**12b**).—Methyltriphenylphosphonium bromide (0.62 g, 1.74 mmol) was dissolved in dry diethyl ether and the solution was stirred under nitrogen at room temperature. n-Butyl-lithium (1.34M in hexane; 1.2 ml, 1.61 mmol) was added dropwise, and the resulting deep orange solution was stirred for 10 min. A solution of methyl 3-*O*-benzyl-2-deoxy-6-*O*-(diphenyl-t-butylsilyl)-2-*C*-methyl-α-D-*arabino*-hexopyranosid-4-ulose (**11b**) (0.76 g, 1.47 mmol) in dry diethyl ether (10 ml) was then added dropwise. After 45 min, t.l.c. [light petroleum–ethyl acetate (10:1)] showed that no starting material remained, and the reaction was quenched with water. The mixture was diluted with brine, the product was extracted into diethyl ether, and the extract was dried over potassium carbonate and concentrated under reduced pressure. Repeated column chromatography gave the title product as an oil [light petroleum–ethyl acetate (12:1)] (0.43 g, 57%).

Methyl 3-O-*Benzyl*-2,4-*dideoxy*-2-C-*methyl*-4-C-*methylene*-6-O-*trityl*-α-D-arabino-*hexopyranoside* (**12a**).—Methyltriphenylphosphonium bromide (2.0 g, 5.7 mmol) was dissolved in dry diethyl ether (100 ml) and the solution was stirred under nitrogen at room temperature. n-Butyl-lithium (1.19M in hexane; 5.0 ml, 5.95 mmol) was added dropwise, and the mixture was refluxed for 1 h. A solution of methyl 3-*O*-benzyl-2-deoxy-2-*C*-methyl-6-*O*-trityl-α-D-*arabino*-hexopyranosid-4-ulose (**11a**) (2.3 g, 4.37 mmol) in dry diethyl ether (20 ml) was added, and the mixture was refluxed for 2 h, after which t.l.c. [light petroleum–ethyl acetate (3:1)] showed that a new, higher-R_F product had been formed. The reaction was quenched with water, and the mixture was diluted with brine. The product was extracted (Et_2O), and the extract was dried over sodium sulphate and concentrated under reduced pressure. Flash chromatography [light petroleum–ethyl acetate (12:1)] gave the title product (**12a**) as an oil (1.9 g, 84%), $[\alpha]_D^{20}$ +30.78° (*c* 1.15 in $CHCl_3$); δ_H 0.99 [3 H, d, *J* 7.2 Hz (dec. at δ 2.2, s), 2-Me], 2.01 [1 H, m (dec. at δ 3.6, dq, J_q 7.2, J_d 2.3 Hz), 2-H], 3.36 (2 H, m, 6-H_2), 3.46 (3 H, s, OMe), 3.66 [1 H, br d, *J* 5.5 (dec. at δ 2.2, br s), 3-H], 4.36 and 4.64 (2 H, AB, *J* 12.4 Hz, PhCH_2), 4.49 [1 H, d, *J* 2.3 Hz (dec. at δ 2.2, s), 1-H], 4.61 (1 H, m, 5-H), 4.91 and 5.01 (both 1 H, br s, C=CH_2), and 7.2—7.3 (20 H, m, 4 × Ph); δ_C 15.9 (2-Me), 42.0 (C-2), 55.4 (OMe), 65.3 (C-6), 69.3 and 70.9 (C-3 and PhCH_2), 80.5 (C-5), 86.9 (Ph_3C), 104.2 (C-1), 110.4 (C=CH_2), 126—142 (aromatics), and 138.5 (C-4).

Methyl 3-O-*Benzyl*-2-*deoxy*-6-O-(*diphenyl-t-butylsilyl*)-2-C-*methyl*-4-C-(*trimethylsilylmethyl*)-α-D-*altro- and -ido-pyranoside* (**20**) *and* (**21**).—(Chloromethyl)trimethylsilane (0.88 g, 7.2 mmol) was added to magnesium turnings (pre-activated by iodine; 2.8 g, 10.0 mmol based on m.w. of MgI_2), in dry diethyl ether (30 ml) under nitrogen. After 1 h, a solution of methyl 3-*O*-benzyl-2-deoxy-6-*O*-(diphenyl-t-butylsilyl)-2-*C*-methyl-α-D-*arabino*-hexopyranosid-4-ulose (0.79 g, 1.52 mmol) in dry diethyl ether (12 ml) was added, and the mixture was stirred for 12 h. The reaction mixture was then poured into water and the product was extracted (Et_2O). The extract was dried over sodium sulphate, and was then concentrated under reduced pressure (0.9 g, quantitative). Two products were isolated by flash chromatography [light petroleum–ethyl acetate (8:1)]. The first fraction was methyl 3-*O*-benzyl-2-deoxy-6-*O*-(diphenyl-t-butylsilyl)-2-*C*-methyl-4-*C*-(trimethylsilylmethyl)-α-D-idopyranoside (**21**). (0.21 g, 23%), $\nu_{max.}$(film) 3 495 cm^{-1} (O–H); δ_H 0.02 (9 H, s, $SiMe_3$), 1.08 (9 H, s, Bu^t), 1.13 (3 H, d, *J* 6.9 Hz, 2-Me), 1.02 and 1.40 (2 H, AB, *J* 15 Hz, CH_2SiMe$_3$), 1.92 (1 H, m, 2-H), 2.96 (1 H, s, OH), 3.38 (3 H, s, OMe), 3.39 (1 H, d, *J* 8.0 Hz 3-H), 3.87 (1 H, m, 5-H), 4.02 and 3.97 (2 H, ABd, J_{AB} 11.3, J_{ax} 4.8, J_{eq} 3.7 Hz, 6-H_2), 4.48 (1 H, d, *J* 5.9 Hz, 1-H), 4.66 and 4.69 (2 H, AB, *J* 11.7 Hz, PhCH_2), and 7.30—7.52 and 7.7—7.8 (15 H, m, 3 × Ph); δ_C 0.7 (q, $SiMe_3$), 15.2 (q, 2-Me), 19.1 (s, CMe_3), 22.9 (t, CH_2SiMe_3), 26.8 (q, CMe_3), 38.2 (d, C-2), 55.9 (q, OMe), 63.9 (t, C-6), 73.7 (t, PhCH_2), 75.5 and 84.6 (both d, C-3 and -5), 77.1 (s, C-4), 103.7 (d, C-1), and 127.5—138.9 (aromatics).

The second fraction was methyl 3-*O*-benzyl-2-deoxy-6-*O*-(diphenyl-t-butylsilyl)-2-*C*-methyl-4-*C*-(trimethylsilylmethyl)-α-D-altropyanoside (**20**) (0.17 g, 18%), $\nu_{max.}$(film) 3 505 cm^{-1} (O–H); δ_H −0.14 (9 H, s, $SiMe_3$), 0.82 and 0.88 (2 H, AB, *J* 15 Hz, CH_2SiMe$_3$), 1.08 (9 H, s, Bu^t), 1.14 (3 H, d, *J* 7.3 Hz, 2-Me), 2.22 (1 H, d, 2-H), 2.77 (1 H, s, OH), 3.37 (1 H, d, *J* 6.2 Hz, 3-H), 3.58 (3 H, s, OMe), 3.78 (1 H, dd, *J* 7.0 and 11.0 Hz, 5-H), 3.98 (2 H, m, 6-H_2), 4.64 (1 H, d, *J* 4.4 Hz, 1-H), 4.60 and 4.79 (2 H, AB, *J* 11.7 Hz, PhCH_2), and 7.3—7.8 (15 H, m, 3 × Ph); δ_C 0.8 (q, CMe_3), 16.1 (q, 2-Me), 19.0 (s, CMe_3), 22.6 (t, CH_2SiMe_3), 26.9 (q, $SiCMe_3$), 37.5 (d, C-2), 55.5 (q, OMe), 64.2 (t, C-6), 72.5 (s, C-4), 73.8 (t, PhCH_2), 76.0 and 84.3 (both d, C-3 and -5), 102.8 (d, C-1), and 127.1—138.0 (aromatics).

Attempted Elimination of Trimethylsilanol from Methyl 3-O-*Benzyl*-2-*deoxy*-6-O-(*diphenyl-t-butylsilyl*)-2-C-*methyl*-4-C-(*trimethylsilylmethyl*)-α-D-*idopyranoside* (**21**).—Methyl 3-*O*-benzyl-2-deoxy-6-*O*-(diphenyl-t-butylsilyl)-2-*C*-methyl-4-*C*-(trimethysilylmethyl)-α-D-idopyranoside (**21**) (0.014 g, 0.023 mmol) was dissolved in dry THF (3 ml) and the solution was added to potassium hydride (35% dispersion in oil, pre-washed with light petroleum; 0.0053 g, 0.046 mmol). The reaction mixture was stirred until the starting material was no longer visible by t.l.c. [light petroleum–ethyl acetate (5:1)]. The reaction was quenched with water and the product was extracted into dichloromethane. The resulting solution was dried over sodium sulphate, and concentrated under reduced pressure. No identifiable product could be detected.

Elimination of Trimethylsilanol from Methyl 3-O-*Benzyl*-2-*deoxy*-6-O-(*diphenyl-t-butyl*)-2-C-*methyl*-4-C-(*trimethylsilylmethyl*)-α-D-*altropyranoside* (**20**).—Similar reaction of compound (**20**) (0.026 g, 0.043 mmol) with potassium hydride (35% suspension in oil, pre-washed in light petroleum; 0.0098 g, 0.0086 mmol), and identicial work-up, gave methyl 3-*O*-benzyl-2,4-dideoxy-6-*O*-(diphenyl-t-butylsilyl)-2-*C*-methyl-4-*C*-methylene-α-D-*arabino*-hexopyranoside (**12b**) (0.011 g, 42%).

Hydrogenation of Methyl 3-O-*Benzyl*-2,4-*dideoxy*-2-C-*methyl*-4-C-*methylene*-6-O-*trityl*-α-D-arabino-*hexopyranoside* (**12a**).—Methyl 3-*O*-benzyl-2,4-dideoxy-2-*C*-methyl-4-*C*-methylene-6-*O*-trityl-α-D-*arabino*-hexopyranoside (**12a**) (0.21 g, 0.40 mmol) and palladium–charcoal (10%; 0.2 g) were added to ethyl acetate (5 ml) and the mixture was hydrogenated at 50 °C for 1 h. The mixture was then filtered through Celite and the filtrate was concentrated under reduced pressure. Two main products were isolated by p.l.c. [light petroleum–ethyl acetate (7:2)]. The first was *methyl* 2,4-*dideoxy*-2,4-*di*-C-*methyl*-6-O-*trityl*-α-D-*idopyranoside* (**14a**) (0.06 g, 35%), $\nu_{max.}$(film) 3 440 cm^{-1} (O–H); δ_H 0.79 (3 H, d, *J* 7.8 Hz, 2-Me), 1.06 (3 H, d, *J* 7.3 Hz, 4-Me), 1.85 (2 H, m, 2- and 4-H), 3.02 and 3.32 (2 H, ABd, J_{AB} 9.5, J_{ax} 7.3, J_{eq} 4.5 Hz, 6-H_2), 3.43 (1 H, m, 3-H), 3.49 (3 H, s, OMe), 4.26 (1 H, td, *J* 7.3, and 4.5 Hz 5-H), 4.53 (1 H, d, *J* 2.5

Hz, 1-H), and 7.2—7.5 (15 H, m, 3 × Ph); δ_C 12.5 and 15.4 (2- and 4-Me), 37.6 and 39.8 (C-2 and -4), 55.3 (OMe), 64.2 and 66.8 (C-3 and -5), 75.5 (C-6), 86.8 (CPh_3), 103.4 (C-1), 127.0 (*p*-aromatics), 127.8 and 128.7 (*o*- and *m*-aromatics), and 144.1 (*i*-aromatics); *m/z* 432 (M^+) (Found: M^+, 432.2299. $C_{28}H_{32}O_4$ requires *M*, 432.2300).

The second product was the isomeric *methyl* 2,4-*dideoxy*-2,4-*di*-C-*methyl*-6-O-*trityl*-α-D-*altropyranoside* (**13a**) (0.03 g, 17%), δ_H 0.68 (3 H, d, *J* 6.4 Hz, 4-Me), 1.09 (3 H, d, *J* 7.3 Hz, 2-Me), 2.05 (2 H, m, 2- and 4-H), 3.09 and 3.35 (2 H, ABd, J_{AB} 10.1, J_{ax} 5.1, J_{eq} 2.3 Hz, 6-H_2), 3.42 (1 H, m, 3-H), 3.43 (3 H, s, OMe), 3.66 (1 H, ddd, *J* 11.0, 2.3, and 5.1 Hz, 5-H), 4.65 (1 H, s, 1-H), and 7.2—7.54 (15 H, m, 3 × Ph); δ_C 13.6 and 15.1 (2- and 4-Me), 30.6 and 38.6 (C-2 and -4), 54.9 (OMe), 64.6 and 69.2 (C-3 and -5), 74.2 (C-6), 86.4 (CPh_3), 103.3 (C-1), 126.1 (*p*-aromatics), 127.8 and 128.8 (*o*- and *m*-aromatics), and 144.3 (*i*-aromatics); *m/z* 432 (M^+) (Found: M^+, 432.2301).

Methyl 2,4-*Dideoxy*-2,4-*di*-C-*methyl*-6-O-*trityl*-α-D-arabino-*hexopyranosid*-3-*ulose*.—Dry DMSO (2 ml) and dichloromethane (5 ml) were stirred at −60 °C under dry nitrogen, and a solution of oxalyl dichloride (0.15 g, 1.2 mmol) in dry dichloromethane (1 ml) was added dropwise. After 10 min, a solution of methyl 2,4-dideoxy-2,4-di-*C*-methyl-6-*O*-trityl-α-D-altropyranoside (**13a**) (0.077 g, 0.18 mmol) in dry dichloromethane (2 ml) was added dropwise. After 2 h the mixture was poured into triethylamine (1 ml) at room temperature. After a further 10 min the mixture was diluted with water, and the product was extracted into dichloromethane. The extracts were washed with brine, dried over sodium sulphate, and concentrated under reduced pressure. The *title product* (the sole product) was obtained by p.l.c. [light petroleum–ethyl acetate (4:1)] (0.051 g, 66%), $[\alpha]_D^{20}$ +17.3° (*c* 0.4 in $CHCl_3$); $\nu_{max.}$(film) 1 717 cm^{-1} (C=O); δ_H 0.73 (3 H, d, *J* 6.7 Hz, 4-Me), 1.33 (3 H, d, *J* 7.3 Hz, 2-Me), 2.57 (1 H, dq, J_q 7.3, J_d 2.0 Hz, 2-H), 2.86 (1 H, qd, J_q 6.7, J_d 9.0 Hz, 4-H), 3.15 and 3.46 (2 H, ABd, J_{AB} 10.0, J_{ax} 4.7, J_{eq} 2.0 Hz, 6-H_2), 3.40 (3 H, s, OMe), 3.77 (1 H, ddd, *J* 9.0, 2.0, and 4.7 Hz, 5-H), 4.81 (1 H, d, *J* 2.0 Hz, 1-H), 7.2—7.5 (15 H, m, 3 × Ph); *m/z* 430 (M^+) (Found: M^+, 430.2146. $C_{28}H_{30}O_4$ requires *M*, 430.2144).

Methyl 2,4-*Dideoxy*-2,4-*di*-C-*methyl*-6-O-*trityl* -α-D-lyxo-*pyranosid*-3-*ulose*.—Dry DMSO (2 ml) and dichloromethane (5 ml) were stirred at −60 °C under nitrogen, and a solution of oxalyl dichloride (0.15 g, 1.2 mmol) in dichloromethane (1 ml) was added dropwise. A solution of methyl 2,4-dideoxy-2,4-di-*C*-methyl-6-*O*-trityl-α-D-idopyranoside (**14a**) (0.075 g, 0.17 mmol) in dry dichloromethane (2 ml) was added dropwise. After 2 h the reaction mixture was poured into triethylamine (1 ml) at room temperature. After 10 min the mixture was diluted with water, and the product was extracted into dichloromethane. The extracts were washed with brine, dried over sodium sulphate, and concentrated under reduced pressure. A single product was obtained as an *oil* by p.l.c. [light petroleum–ethyl acetate (4:1)] (0.045 g, 62%), $[\alpha]_D^{20}$ +5.36° (*c* 0.56 in $CHCl_3$); $\nu_{max.}$(film) 1 722 cm^{-1} (C=O); δ_H 0.91 (3 H, d, *J* 7.2 Hz, 2-Me), 1.13 (3 H, d, *J* 6.9 Hz, 4-Me), 2.56 (2 H, m, 2-and 4-H), 3.10 and 3.36 (2 H, ABd, J_{AB} 12.0, J_{ax} 7.0, J_{eq} 4.5 Hz, 6-H_2), 3.47 (3 H, s, OMe), 4.53 (1 H, d, *J* 5.5 Hz, 1-H), 4.55 (1 H, m, 5-H), and 7.2—7.5 (15 H, m, 3 × Ph); *m/z* 430 (M^+) (Found: M^+, 430.2145).

Epimerization of Methyl 2,4-*Dideoxy*-2,4-*di*-C-*methyl*-6-O-*trityl*-α-D-arabino-*hexopyranosid*-3-*ulose*.—Methyl 2,4-dideoxy-2,4-di-*C*-methyl-6-*O*-trityl-α-D-*arabino*-hexopyranosid-3-ulose (0.004 g, 0.009 mmol) was dissolved in methanol (1 ml), and sodium methoxide (1M in methanol; 3 drops) was added. The mixture was stirred for 6 h at −78 °C, when t.l.c. [light petroleum–ethyl acetate (5:1)] showed one major and several minor products. The mixture was poured into a phosphate buffer (50 ml), and extracted into dichloromethane; the extracts were dried over anhydrous sodium sulphate and concentrated under reduced pressure. The product (0.003 g, 75%) was used directly in the next step.

Epimerization and Reduction of Methyl 2,4-*Dideoxy*-2,4-*di*-C-*methyl*-6-O-*trityl*-α-D-lyxo-*hexopyranosid*-3-*ulose*.—Methyl 2,4-dideoxy-2,4-di-*C*-methyl-6-*O*-trityl-α-D-*lyxo*-hexopyranosid-3-ulose (0.11 g, 0.25 mmol) was dissolved in methanol (5 ml), and sodium methoxide (1M in methanol; 30 drops) was added. After 12 h at −30 °C, and 6 h at −60 °C, t.l.c. [light petroleum–ethyl acetate (5:1)] showed a similar mixture of products to that obtained from the epimerization of the *arabino* derivative. The reaction mixture was poured into a phosphate buffer (100 ml), and extracted into dichloromethane, and the extract was dried over sodium sulphate and concentrated under reduced pressure (0.088 g, 82%). The product was dissolved in methanol (6 ml), and sodium borohydride (0.008 g, 0.21 mmol) was added. After 30 min the reaction mixture was poured into saturated aq. ammonium chloride, and the product was extracted into dichloromethane. The extract was dried over sodium sulphate and concentrated under reduced pressure (0.088 g, quantitative). Three products were separated by p.l.c. [light petroleum–acetate (3:1)] (0.072 g, 79%). One of the products (0.029 g, 32%) was identified by ^1H n.m.r. spectroscopy as a 2:1 mixture of two compounds, both with equatorial C-2 methyl groups, one with an axial C-4 methyl group, and one with an equatorial C-4 methyl group. The stereochemistry at C-3 was unknown.

Major product: $\nu_{max.}$(film) 3 550 cm^{-1} (O–H); δ_H 0.73 (3 H, d, *J* 7.0 Hz) and 1.09 (3 H, d, *J* 7.0 Hz) (2- and 4-Me), 1.95 (2 H, m, 2- and 4-H), 2.92 (1 H, d, *J* 10.0 Hz, OH), 3.04 and 3.35 (2 H, ABd, J_{AB} 9.5, J_{ax} 5.5, J_{eq} 2.3 Hz, 6-H_2), 3.44 (3 H, s, OMe), 3.53 (1 H, m, 3-H), 3.67 (1 H, ddd, *J* 2.3, 5.5, and 10.0 Hz, 5-H), 4.71 (1 H, d, *J* 2.5 Hz, 1-H), and 7.20—7.54 (15 H, m, 3 × Ph).

Minor product: $\nu_{max.}$(film) 3 550 cm^{-1} (O–H); δ_H 0.71 and 1.02 (each 3 H, d, *J* 7.0 Hz 2- and 4-Me), 1.78 (2 H, m, 2- and 4-H), 2.93 (1 H, d, *J* 10.0 Hz, OH), 3.04 and 3.35 (2 H, ABd, J_{AB} 9.5, J_{ax} 5.5, J_{eq} 2.3 Hz, 6-H_2), 3.47 (3 H, s, OMe), 3.51 (1 H, m, 3-H), 4.24 (1 H, m, 5-H), 4.58 (1 H, d, *J* 2.3 Hz 1-H), and 7.2—7.5 (15 H, m, 3 × Ph).

Methyl 2,3,4-*Trideoxy*-2,4-*di*-C-*methyl*-6-O-*trityl*-α-D-ribo-*hexopyranoside* (**25**).—To sodium hydride (60% dispersion in oil; 0.01 g, 0.23 mmol; pre-washed with light petroleum) was added a solution of the major product from epimerization–reduction procedure (0.02 g, 0.046 mmol) in dry THF (2 ml), followed by carbon disulphide (0.018 g, 0.23 mmol). The mixture was stirred at 35 °C for 4 h, and iodomethane (2 drops was added. After 5 min, the mixture was diluted with water and the product was extracted into dichloromethane. The extract was dried over sodium sulphate and concentrated under reduced pressure to give a yellow oil (0.023 g, 96%). The oil was dissolved in dry toluene (2 ml), and tri-n-butyltin hydride (0.015 g, 0.05 mmol) and an aliquot of azaisobutyronitrile was added. The mixture was refluxed for 2 h. The mixture was then quenched with water, and the product was extracted into dichloromethane. The resulting solution was dried over anhydrous sodium sulphate and concentrated under reduced pressure. Repeated p.l.c. [light petroleum–diethyl ether (8:1), both redistilled] gave a mixture of methyl 2,3,4-trideoxy-2,4-di-*C*-methyl-6-*O*-trityl-α-D-*ribo*-and -*xylo*-hexopyranoside (2:1; 4.6 mg, 23%); δ_H (*ribo* derivative) 0.61 (3 H, d, *J* 6.5 Hz, 4-Me), 0.88 (3 H, d, *J* 6.9 Hz, 2-Me), 1.8 (4 H, m, 2- and 4-H, and 3-H_2), 3.08 and 3.25 (2 H, ABd, J_{AB} 10.0, J_{ax} 5.8, J_{eq} 1.4 Hz, 6-H_2), 3.43 (3 H, s, OMe), 3.42 (1 H, m, 5-H), 4.57 (1 H, d, *J* 3.3 Hz 1-H), and 7.20—7.54 (15 H, m, 3 × Ph).

δ_H (*xylo* Derivative) 0.76 (3, H, d, *J* 7.0 Hz, 4-Me), 0.84 (3 H, d, *J* 6.7 Hz, 2-Me), 1.8 (4 H, m, 2- and 4-H, and 3-H_2), 2.84 and 3.25 (2 H, ABd, J_{AB} 10.0, J_{ax} 5.8 J_{eq} 1.4 Hz, 6-H_2), 3.43 (3 H, s, OMe), 4.05 (1 H, m, 5-H), 4.47 (1 H, d, *J* 3.2 Hz, 1-H), and 7.20—7.54 (15 H, m, 3 × Ph).

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